Complete Summary

GUIDELINE TITLE

Idiopathic thrombocytopenic purpura: a practice guideline developed by explicit methods for the American Society of Hematology.

BIBLIOGRAPHIC SOURCE(S)

George JN, Woolf SH, Raskob GE, Wasser JS, Aledort LM, Ballem PJ, Blanchette VS, Bussel JB, Cines DB, Kelton JG, Lichtin AE, McMillan R, Okerbloom JA, Regan DH, Warrier I. Idiopathic thrombocytopenic purpura: a practice guideline developed by explicit methods for the American Society of Hematology. Blood 1996 Jul 1;88(1):3-40. [295 references] PubMed

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Idiopathic Thrombocytopenic Purpura (ITP)

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management

CLINICAL SPECIALTY

Family Practice
Hematology
Internal Medicine
Obstetrics and Gynecology
Pediatrics

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To issue explicitly developed practice recommendations, based as much as possible on published, scientific evidence, regarding the diagnosis and treatment of patients with known or suspected idiopathic thrombocytopenic purpura.

TARGET POPULATION

- Adults and children with known or suspected idiopathic thrombocytopenic purpura (ITP)
- Pregnant women with known or suspected ITP
- Newborns of mothers with ITP

INTERVENTIONS AND PRACTICES CONSIDERED

Refer to the "Major Recommendations" field for details about the appropriate use of the following interventions considered by the guideline developers:

Children

Diagnosis

1. History
2. Physical examination
3. Complete blood count
4. Examination of the peripheral smear
5. Bone marrow aspiration

Treatment

1. Hospitalization
2. Conventional critical care measures
3. Observation (no specific initial treatment)
4. Glucocorticoids
5. Intravenous immunoglobulin (IVIg)
6. Anti-Rh(D)
7. Splenectomy
8. Platelet transfusion

Adults

Diagnosis

1. History
2. Physical examination
3. Complete blood count
4. Examination of the peripheral smear
5. Bone marrow aspiration

Treatment

1. Hospitalization
2. Conventional critical care measures
3. Observation (no specific initial treatment)
4. Glucocorticoids
5. IVIg
6. Anti-Rh(D)
7. Splenectomy
8. Platelet transfusion

Pregnant Women

Diagnosis

1. History, physical examination and CBC
2. Blood pressure measurement
3. Liver function testing
4. HIV antibody test for patients with risk factors for HIV infection

Treatment

1. Observation (no specific initial treatment)
2. Glucocorticoids
3. IVIg
4. Splenectomy
5. Percutaneous umbilical vein blood sampling (PUBS); fetal scalp vein sampling
6. Cesarean or vaginal delivery
7. Prophylactic platelet transfusion

Newborns (of Mothers With Idiopathic Thrombocytopenic Purpura [ITP])

Diagnosis

1. Neonatal platelet count
2. Brain imaging (eg, ultrasound)

Treatment

1. Observation
2. IVIg
3. Combined glucocorticoid and IVIg therapy

MAJOR OUTCOMES CONSIDERED

Efficacy of treatment of idiopathic thrombocytopenic purpura (ITP):

- Surrogate outcome: platelet count
- Health outcomes: bleeding, death

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

A computerized search of the MEDLINE (U.S. National Library of Medicine) database, performed in April 1994, sought English-language articles published between 1966 and 1994. Search terms (Medical Subject Headings) included: "THROMBOCYTOPENIA," "PLATELET COUNT," "AUTOIMMUNE THROMBOCYTOPENIC PURPURA," "COMPLETE BLOOD COUNT," "BONE MARROW EXAMINATION," "RETICULOCYTE COUNT," "ANTINUCLEAR ANTIBODY TEST," "IGG," "DIAGNOSIS (SH)," and "THERAPY (SH)." The database was also searched on the text word "ITP." The computerized search retrieved 581 articles. This initial reference list underwent substantial expansion after being supplemented with relevant articles from the files of panel members, publications from 1989 through 1995 retrieved with alternate search software ("Reference Update" Institute for Scientific Information, Inc.), and cross-checking against the bibliographies of retrieved articles to identify additional publications (especially those published before 1966). Case reports, case series of less than five patients, review articles, and letters-to-the-editor without primary data were excluded from review. Statements in the original guideline about the number of studies that have examined the efficacy of specific treatments and statements that "no published evidence is available" do not include case reports and other categories of inadmissible evidence.

NUMBER OF SOURCE DOCUMENTS

More than 580 documents

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Level of Evidence Study Design

I. Strongest Randomized trials with low false-positive and false-negative errors.
II. Randomized trials with high false-positive and false-negative errors.

III. Nonrandomized studies with concurrent control group.
IV. Nonrandomized studies with historical control group.
V. Weakest Case series without a control group.

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Each article was evaluated independently by two panel members (James N. George, Gary E. Raskob) to assess scientific validity and verify results. Scientific validity was assessed using published guidelines. Literature on the clinical course of idiopathic thrombocytopenic purpura (ITP) was evaluated for the presence of an inception cohort of consecutive patients, an explicit referral pattern, complete follow-up, and use of objective outcome criteria. The term "inception cohort" refers to a group of patients identified at an early and uniform point in the course of their disease so that patients who die or completely recover are included with patients in whom the disease persists. Most of the ITP literature reviewed in this report pertains to therapy. The strength of the evidence for individual therapeutic approaches was assessed using the "level of evidence" criteria outlined in the NGC Complete Summary, "Rating Scheme" field (see also, Table 1 in the original guideline document). Evidence tables in the Results section of the guideline document only present data from Level I and Level II studies.

For those therapies for which only Level V evidence is available, or for which no evidence is available, and for issues on diagnosis that have not been addressed by clinical studies, the opinion of the panel was assessed. Survey instruments were used to assess quantitatively the opinion and strength of consensus of the panel, and these data provide the basis for statements about opinion in the text and tables.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Nominal Group Technique)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Survey instruments were designed at panel meetings in which members were asked to identify the key diagnostic and treatment practices for which opinion would be assessed. The appropriateness of these practices was intentionally not discussed at the meeting to avoid influencing the responses by the opinions of more assertive panel members. A 41-page questionnaire addressing these practices was mailed to panel members in 1994 to be completed independently, without discussion with one another. The questionnaire, which included separate pediatric and adult sections, asked respondents to measure the necessity and appropriateness of diagnosis or treatment in over 1,300 clinical scenarios. In these surveys, "Necessary" was defined as a test or treatment that should be performed; "Appropriate" was defined as a test or treatment that may or may not be necessary, but performing it is not wrong; "Unnecessary" was defined as a test

or treatment that need not be performed, but is not necessarily inappropriate; "Inappropriate" was defined as a test or treatment that should not be performed.

Questions relating to adult patients were completed by 11 panel members, and questions relating to pediatric patients were completed by six respondents. A second, 25-page questionnaire was circulated in early 1995 to examine opinions regarding pregnancy and newborn care and to clarify opinions regarding issues identified in the 1994 survey. The 1995 survey examined over 600 issues and was completed by 13 panel members.

Using a modified RAND scoring system, the questionnaire asked panelists to quantify the strength of their opinion on a 1 to 9 scale; "9" represented strong agreement with the appropriateness/necessity of the practice and "1" represented strong disagreement. The mean response for each question provided an overall assessment of the panel's opinion regarding the necessity and appropriateness of specific practices. Panel votes are presented in this report only when there was agreement among the panel regarding the necessity or appropriateness of an intervention (mean panel score of 7.0 to 9.0) or agreement that the intervention is unnecessary or inappropriate (mean panel score of 1.0 to 3.0).

The strength of the panel's inter-observer agreement about the appropriateness/necessity of tests or treatments was graded using the standard deviations (SDs) for responses to each question (see Table 2 in the guideline document). Panel responses were classified as category A ("Complete or Almost Complete Unanimity"), for example, if the variance in panel member responses to a specific question was more than two SDs below the mean variance. Thus, a score of "1.5, A" signified strong agreement among the panel that the intervention is unnecessary/inappropriate, with most panelists assigning scores close to 1.0. A score of 7.5, D meant that, on average, the panel considered the intervention necessary/appropriate, but that wide variation in the responses of individual panel members was noted. These scores were arbitrarily considered as representing a consensus if the mean score was 3 or less or 7 or more.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Before the final panel meeting, the report was independently reviewed by eight private practice and university-based hematologists with expertise in adult and/or pediatric idiopathic thrombocytopenic purpura (ITP).

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Children

Diagnosis

The diagnosis of idiopathic thrombocytopenic purpura (ITP) is based principally on the history, physical examination, complete blood count, and examination of the peripheral smear, which should exclude other causes of thrombocytopenia. Further diagnostic studies are generally not indicated in the routine work-up of patients with suspected ITP, assuming that the history, physical examination, and blood counts are compatible with the diagnosis of ITP and do not include atypical findings that are uncommon in ITP or suggest other etiologies. Patients with risk factors for human immunodeficiency virus (HIV) infection should be tested for HIV antibody, and an abdominal computed tomographic (CT) scan or ultrasound examination is appropriate in patients with suspected splenomegaly on initial physical examination. Bone marrow aspiration should be performed to establish the diagnosis in patients with persistent thrombocytopenia (lasting more than 6 to 12 months) and in those unresponsive to intravenous Ig (IVIg), but it should not be performed to establish the diagnosis before initiating IVIg therapy. Additional testing is also generally unnecessary, and sometimes inappropriate, when performed on a routine basis to establish the diagnosis before splenectomy or to evaluate patients who have not responded to glucocorticoid therapy, IVIg, and splenectomy.

Treatment

Children with platelet counts >30,000 should not be hospitalized and do not routinely require treatment if they are asymptomatic or have only minor purpura; they should not be given glucocorticoids, IVIg, or anti-Rh(D) as routine initial treatment. Children with platelet counts <20,000 and significant mucous membrane bleeding and those with counts <10,000 and minor purpura should be treated with specific regimens of IVIg or glucocorticoids. Patients with severe, life-threatening bleeding should be hospitalized and receive conventional critical care measures, along with treatment for ITP: appropriate regimens include high-dose parenteral glucocorticoid therapy, IVIg, and platelet transfusions.

Splenectomy is clearly appropriate or inappropriate in specific clinical situations. If an elective splenectomy is planned, appropriate preoperative therapy includes prophylactic IVIg therapy for patients with platelet counts <30,000, and IVIg, parental glucocorticoids, and anti-Rh(D) for patients with platelet counts <10,000. Inappropriate preoperative prophylaxis includes IVIg, oral glucocorticoid therapy, or anti-Rh(D) when platelet counts exceed 50,000, parenteral glucocorticoid therapy when platelet counts exceed 30,000, and platelet transfusions when platelet counts exceed 20,000.

When ITP symptoms persist after primary treatment (glucocorticoid, IVIg) and splenectomy, further treatment is indicated in children with platelet counts <30,000 who have active bleeding. Panel members suggested many treatments

as reasonable options but did not reach consensus on any single regimen, reflecting the lack of evidence that any single treatment is more effective than another.

Adults

Diagnosis

The diagnosis of ITP is based principally on the history, physical examination, complete blood count, and examination of the peripheral smear, which should exclude other causes of thrombocytopenia. Further diagnostic studies are generally not indicated in the routine work-up of patients with suspected ITP, assuming that the history, physical examination, and blood counts are compatible with the diagnosis of ITP and do not include atypical findings that are uncommon in ITP or suggest other etiologies. Patients with risk factors for HIV infection should be tested for HIV antibody. Bone marrow aspiration is appropriate to establish the diagnosis in patients over age 60 and in patients considering splenectomy. Additional testing is also generally unnecessary, and sometimes inappropriate, when performed on a routine basis to establish the diagnosis before splenectomy or to evaluate patients who have not responded to glucocorticoid therapy and splenectomy. Preoperative thyroid function testing is appropriate to rule out occult hyperthyroidism or hypothyroidism before elective splenectomy.

Treatment

Patients with platelet counts >20,000 should not be hospitalized if they are either asymptomatic or have only minor purpura. Patients with counts >50,000 do not routinely require treatment; they should not be given glucocorticoids or IVIg as routine initial treatment. IVIg is also inappropriate as initial treatment in patients with counts >30,000 who are asymptomatic or have only minor purpura. However, treatment is indicated in patients with platelet counts <20,000 to 30,000, and those with counts <50,000 and significant mucous membrane bleeding (or risk factors for bleeding, such as hypertension, peptic ulcer disease, or a vigorous lifestyle). Initial therapy with glucocorticoids (e.g., prednisone) is appropriate in such patients. Hospitalization is appropriate for patients with platelet counts <20,000 who have significant mucous membrane bleeding. Patients with severe, life-threatening bleeding should also be hospitalized and should receive conventional critical care measures, along with treatment for ITP: appropriate regimens include high-dose parenteral glucocorticoid therapy, IVIg, and platelet transfusions.

Splenectomy is clearly appropriate or inappropriate in specific clinical situations. It should not be performed as initial therapy in patients who have no bleeding, minor purpura, or even mucous membrane bleeding. In a patient who has had bleeding symptoms (e.g., epistaxis, menorrhagia), splenectomy is often appropriate if platelet counts remain below 30,000 after 4 to 6 weeks of medical treatment. If an elective splenectomy is planned, appropriate preoperative therapy includes prophylactic IVIg or oral glucocorticoid therapy for patients with platelet counts <20,000. Inappropriate preoperative prophylaxis includes IVIg, oral or parenteral glucocorticoid therapy, and anti-Rh(D) when platelet counts exceed 50,000, and platelet transfusions when platelet counts exceed 10,000.

When ITP symptoms persist after primary treatment (glucocorticoid) and splenectomy, further therapy is recommended in patients with platelet counts <30,000 who have active bleeding. The most commonly recommended first-choice treatment options include IVIg, glucocorticoids, accessory splenectomy, and no additional treatment, but other agents may also be appropriate (see text). Women with ITP who are of childbearing age and have counts <10,000 after splenectomy and other treatments should be discouraged from becoming pregnant.

Pregnant Women

Diagnosis

The diagnosis of ITP during pregnancy generally does not require special laboratory testing. The patient's blood pressure should be measured to rule out preeclampsia as an alternative diagnosis; liver function testing is also appropriate. Patients with risk factors for HIV infection should be tested for HIV antibody.

Treatment

Recommendations for pregnant women are different from other adults in some situations. Pregnant women with ITP and platelet counts >50,000 do not routinely require treatment and should not receive glucocorticoids or IVIg as routine initial therapy. Women with counts of 30,000 to 50,000 in the first or second trimester also should not receive routine initial treatment. Treatment is required for women with platelet counts <10,000, and for those with platelet counts of 10,000 to 30,000 who are in their second or third trimester or are bleeding. IVIg is appropriate initial treatment for women with platelet counts <10,000 in the third trimester, and for those with counts of 10,000 to 30,000 who are bleeding. In pregnant women who have failed glucocorticoid and IVIg therapy, splenectomy is appropriate in the second trimester in women with platelet counts <10,000 who are bleeding. Splenectomy should not be performed in asymptomatic pregnant women with platelet counts >10,000.

As labor and delivery approach, women with ITP do not require testing for maternal platelet antibodies. Percutaneous umbilical vein blood sampling (PUBS) or fetal scalp vein sampling to measure the fetal platelet count and predict the risk of neonatal bleeding are not necessarily required. PUBS and fetal scalp vein sampling are unnecessary in pregnant women without known ITP even with platelet counts as low as 40,000 at term. Women with ITP should be delivered by cesarean section in selected circumstances (see text). In general, assuming the fetal platelet count (and the platelet count of previous babies) is unknown, cesarean section is not indicated when the maternal platelet count is >50,000. If the fetal platelet count is known, cesarean section is appropriate if the fetal count is <20,000. A maternal platelet count of >50,000 is considered sufficient to prevent complications from excessive maternal bleeding at vaginal delivery or cesarean section. Prophylactic platelet transfusions before delivery are appropriate in women with counts <10,000 who (1) have a planned cesarean section or (2) have epistaxis or other mucous membrane bleeding and are expected to deliver vaginally, but are unnecessary in women with platelet counts >30,000 and no bleeding symptoms.

Newborns (of Mothers With ITP)

Diagnosis

The neonatal platelet count should generally be measured for 3 to 4 days after birth. Brain imaging (e.g., ultrasound) should be performed if the platelet count at birth is <20,000; brain imaging is also appropriate if the count is 20,000 to 50,000, even in the absence of neurologic abnormalities.

Treatment

In newborns without evidence of intracranial hemorrhage (ICH), treatment with IVIg is appropriate if the infant's platelet count is <20,000. Newborns with platelet counts of 20,000 to 50,000 do not necessarily require IVIg treatment. Newborns with counts >50,000 should not be treated with IVIg or glucocorticoids. Newborns with imaging evidence of ICH should be treated with combined glucocorticoid and IVIg therapy if the platelet count is <20,000; they should not be treated with glucocorticoids alone. Women with ITP should not be discouraged from breast-feeding.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

In almost all aspects of idiopathic thrombocytopenic purpura (ITP), level I evidence is lacking, and there are few level II, III, or IV studies to allow firm, evidence-based recommendations (Refer to "Rating Scheme" field in the NGC Complete Summary for definitions of levels of evidence). In general, only level V evidence, or no evidence, was available for making recommendations. Therefore, the panel issued recommendations based on opinion, indicating the mean panel score and variance to permit readers to judge the strength of the consensus. Although the sample sizes of voting members were small and some confidence intervals for panel votes were wide, the results can help readers assess the strength of opinion behind specific recommendations.

Essentially all evidence regarding the efficacy of treatment of ITP is indirect, inferred by measuring a surrogate outcome, platelet count, rather than a health outcome such as bleeding or mortality. Even an effect on the platelet count is difficult to validate convincingly based on currently available data, because evidence of treatment efficacy consists largely of reports from uncontrolled case series.

The basis of recommendations is explicitly labeled in the text of the guideline document so that readers can appreciate which recommendations are based on evidence and which are based on opinion. A synopsis of the type of evidence supporting specific recommendations is given below.

Synopsis:

Children

Diagnosis

In the absence of scientific evidence on the accuracy or effectiveness of diagnostic tests for ITP, the panel's recommendations regarding the history, physical examination, laboratory tests, and special procedures are based entirely on opinion.

Treatment

Hospitalization. There have been no studies to evaluate the effectiveness of hospitalizing children with ITP. The panel's recommendations are based on opinion.

Emergency Treatment. There have been no studies to evaluate the effectiveness of different regimens for the emergency treatment of bleeding. The panel's recommendations are based on opinion.

Observation (No Specific Initial Treatment). Two level I studies and many level V studies

Glucocorticoid therapy. Efficacy: Level I and II studies (summarized in evidence table in guideline document); Specific regimens: several level I, II, III and V studies

IVIg. Efficacy: One level I study, five level V studies (summarized in evidence table in guideline document)

Anti-Rh(D). Efficacy: one level I study (summarized in evidence table in guideline document)

Splenectomy. Efficacy: Sixteen case series (level V evidence)

Alternative treatment modalities (plasma infusion, azathioprine, danazol, and interferon). Efficacy: four level V studies

Adults

Diagnosis

In the absence of scientific evidence on the accuracy or effectiveness of diagnostic tests for ITP, the panel's recommendations regarding the history, physical examination, laboratory tests, and special procedures are based entirely on opinion.

Treatment

Hospitalization. There have been no studies to evaluate the effectiveness of hospitalizing adults with ITP. The panel's recommendations are based on opinion.

Emergency treatment. There have been no studies to evaluate the effectiveness of different regimens for the emergency treatment of severe bleeding. The panel's recommendations are based on opinion.

Observation (No Specific Initial Treatment). One level V, prospective study.

Glucocorticoid therapy. Efficacy: Twelve uncontrolled case series (level V evidence, summarized in an evidence table in the guideline) document; Specific regimens: three level II studies.

IVIg. Nineteen case series (level V evidence).

Anti-(Rh) D: Five level V studies

Splenectomy: Thirty six case series (level V evidence)

Other Treatments:

Splenic radiation, two level V studies

Partial splenic embolization, one level V study

Azathioprine: four case series (level V evidence)

Cyclophosphamide: Five case series (level V evidence)

Danazol: fourteen case series (level V evidence)

Ascorbic acid (vitamin C): Eight case series (level V evidence)

Colchicine: Two conflicting case series (level V evidence)

Plasma exchange: Three case series (level V evidence)

2-Chlorodeoxyadenosine: one case series (level V evidence)

Combination chemotherapy: One case series (level V evidence)

Interferon-(alpha): Four case series (level V evidence)

Cyclosporine A: No published evidence met the panel criteria.

Aminocaproic acid: One case series (level V evidence)

Pregnant women

Diagnosis

In the absence of published evidence, the panel's recommendations are based on opinion.

Treatment

In the absence of published evidence, the panel's recommendations are based on opinion.

Newborns of Mothers with ITP

Diagnosis

In the absence of published evidence, the panel's recommendations are based on opinion.

Treatment

In the absence of published evidence, the panel's recommendations are based on opinion.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Appropriate utilization of tests to establish the diagnosis of idiopathic thrombocytopenic purpura (ITP) in all patients at presentation
- Effective and appropriate management of ITP
- Benefits of specific interventions, summarized below. [Note: Evidence of benefits in terms of morbidity (eg. bleeding) or mortality is lacking for most interventions. Refer to guideline document for further discussion of potential benefits and appropriate indications for various treatment interventions.]

  Children

  Observation (no specific initial treatment). Two level I studies and many level V studies suggest that 30-70% of children recover from severe thrombocytopenia, achieving platelet counts of 50,000 to 100,000 within 3 weeks without specific treatment. Current evidence is inadequate to recommend which groups of children with ITP can be safely managed without therapy.

  Glucocorticoids: There is level I evidence that children with acute ITP and severe thrombocytopenia experience more rapid recovery of platelets if given glucocorticoids, but it is unknown if this influences morbidity or mortality.

  IVIg: There is level I evidence that children with acute, previously untreated ITP experience more rapid recovery of platelets with IVIg than with glucocorticoids or no specific therapy, but it is unclear whether this

enhancement of platelet recovery influences bleeding or mortality or if there are circumstances in which disadvantages of IVIg might outweigh its benefits.

Splenectomy: Data from sixteen case series (level V evidence) show that most children (72% of the 271 children undergoing elective splenectomy) achieve a complete remission from ITP after splenectomy.

Adults

Glucocorticoid therapy: There is consistent level V evidence that glucocorticoids can achieve early responses, most of which are transient.

Splenectomy: Although all available evidence is level V, the efficacy of splenectomy is supported by the consistent incidence of sustained normalization of platelet counts in patients who had previously been refractory to glucocorticoid therapy for several weeks or years.

POTENTIAL HARMS

1. Glucocorticoids: The potential adverse effects of glucocorticoid therapy include all of the signs and symptoms of hypercortisolism in Cushing syndrome, including facial swelling, weight gain, hyperglycemia, hypertension, cataracts, and behavioral abnormalities. The toxicities of glucocorticoids are dose and duration dependent. In children, glucocorticoid therapy may increase the risk of growth retardation. In adults, the greatest risk may be the development of osteoporosis; although there are no data in patients with idiopathic thrombocytopenic purpura (ITP). An objective decrease in bone density has been documented in patients with rheumatoid arthritis after the equivalent of only 10 mg of prednisone daily for 20 weeks.
2. IVIg: Adverse effects of IVIg are common (15% to 75%) but generally mild, including headache, backache, nausea, and fever. Aseptic meningitis may occur. Rare reported complications include alloimmune hemolysis and hepatitis C infection. No hepatitis C has been reported with viral inactivated products. Other complications have been reported in adults. Cases of renal failure, pulmonary insufficiency, and thrombosis, including stroke and myocardial infarction have been reported as complications of IVIg treatment.
3. Splenectomy: The potential adverse effects of splenectomy include the operative and postoperative complications of bleeding and infection. An important concern for late morbidity and mortality after splenectomy is the long-term risk of fatal bacterial infection, particularly in children less than 5 years old, in whom the risk may be 1 death per 300 to 1,000 patient-years. In adults, even in the face of severe thrombocytopenia, the immediate risks of clinically important intraoperative and postoperative hemorrhage appear small, approximately 1% in the 36 cited case series. Operative mortality rates were less than 1%, an impressive figure because these data include reports before the advent of platelet transfusions, IVIg, and effective antibiotics to manage postoperative infections. Most operative deaths occur in older patients with coexisting illnesses. Postoperative morbidity may be related to the extent of previous glucocorticoid therapy. Splenic or portal vein thrombosis may occur after splenectomy. Postsplenectomy patients have a small but significantly increased susceptibility to fatal bacterial infection, although this appears to be less important in adults than in children. The

estimated risk of fatal bacterial infection in splenectomized adults is about 1 per 1,500 patient-years, but these estimates are from the era before immunization for S. pneumoniae and were determined in patients splenectomized for other diseases.

4. Special considerations: In pregnant women, glucocorticoids are considered safe in terms of potential teratogenicity but may have other fetal toxicities. In the mother they may exacerbate gestational diabetes mellitus and postpartum psychiatric disorders. IVIg is considered to be safe for the fetus, having only adverse effects for the mother as described above. Cytotoxic agents such as cyclophosphamide, vinca alkaloids, and azathioprine are avoided during pregnancy because of an assumed risk of teratogenicity, although there are few data regarding the magnitude of the risk. Splenectomy may increase the risk of preterm labor during the first trimester and can be technically difficult because of the size of the uterus in the third trimester, but data regarding the magnitude of risk are lacking.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

1. Idiopathic thrombocytopenic purpura (ITP), also known as primary immune thrombocytopenic purpura) is a hematologic disorder for which appropriate diagnostic and treatment strategies are uncertain.
2. Due to the limited availability of scientific evidence in almost all aspects of ITP, the panel issued recommendations based on opinion, indicating the mean panel score and variance to permit readers to judge the strength of the consensus. The basis of recommendations is explicitly labeled in the text so that reader can appreciate which recommendations are based on evidence and which are based on opinion. The inherent weakness of opinion-based recommendations is acknowledged; these recommendations should not form the basis for definitive decisions on health care policy. Indications for which the panel could not reach consensus are generally not listed in the text; thus, recommendations frequently address only the "extremes" of inappropriate and appropriate practice and do not comment on intermediate clinical scenarios that may be common. The fact that the panel did not reach consensus regarding these indications does not necessarily signal the appropriateness or inappropriateness of clinicians' decisions to administer tests or treatments in these settings.
3. Although these views reflect opinion more than science, the panel believes that a structured approach to defining and expressing its opinion is more precise and less subject to bias than arriving at recommendations through open discussion, in which decisions are more likely to be influenced by the opinions of more assertive panel members.
4. This practice guideline describes a range of approaches to the diagnosis and management of ITP. Its recommendations are not intended to serve as inflexible rules, and they are not inclusive of all proper methods of care or other methods of care that may achieve similar results. Adherence to the guideline will not ensure a successful outcome in every case. The ultimate judgment regarding the care of a particular patient should be made by the physician in light of the clinical data and circumstances presented by the patient and the diagnostic and treatment options available.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Safety

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

George JN, Woolf SH, Raskob GE, Wasser JS, Aledort LM, Ballem PJ, Blanchette VS, Bussel JB, Cines DB, Kelton JG, Lichtin AE, McMillan R, Okerbloom JA, Regan DH, Warrier I. Idiopathic thrombocytopenic purpura: a practice guideline developed by explicit methods for the American Society of Hematology. Blood 1996 Jul 1;88(1):3-40. [295 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1996 Jan 25 (reviewed 2001)

GUIDELINE DEVELOPER(S)

American Society of Hematology - Medical Specialty Society

SOURCE(S) OF FUNDING

American Society of Hematology

GUIDELINE COMMITTEE

ASH Practice Guidelines Panel on ITP

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

The 15-member panel included 13 hematologists selected to represent the ASH membership. The hematologists included both university-affiliated physicians with research interests in idiopathic thrombocytopenic purpura (ITP) and private practitioners. Panel members represented both pediatric and adult medicine perspectives. The panel also included two members with expertise in clinical epidemiology and practice guideline methodology.

Members: James N. George; Steven H. Woolf; Gary E. Raskob; Jeffrey S. Wasser; Louis M. Aledort; Penny J. Ballem; Victor S. Blanchette; James B. Bussel; Douglas B. Cines; John G. Kelton; Alan E. Lichtin; Robert McMillan; John A. Okerbloom; David H. Regan; Indira Warrier

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

ENDORSER(S)

Not applicable

GUIDELINE STATUS

This is the current release of the guideline.

According to the guideline developer, this guideline is reviewed on an annual basis. This review involves updated literature searches of electronic databases and a review of new evidence that has emerged relative to the recommendations presented in the original guideline document. The guideline developer asserts that this guideline is current as of Dec 2001.

An update is not in progress at this time.

GUIDELINE AVAILABILITY

Electronic copies: Available from the American Society of Hematology Web site.

Print copies: Available from the American Society of Hematology, 1200 19th Street, N.W., Third Floor, Washington, DC 20036-2422.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Idiopathic thrombocytopenic purpura: lessons from a guideline. Ann Intern Med 1997 Feb 15;126(4):317-8.
- Diagnosis and treatment of idiopathic thrombocytopenic purpura: recommendations of the American Society of Hematology. Ann Intern Med 1997 Feb 15;126(4):319-26.

- Diagnosis and treatment of idiopathic thrombocytopenic purpura. Am Fam Physician 1996 Dec;54(8):2437-47.

PATIENT RESOURCES

The following is available:

- ITP: what it means to you. Patient information handout. Am Fam Physician 1996 Dec;54(8):2451.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

This summary was completed by ECRI on July 26, 1999. The information was verified by the guideline developer on August 19, 1999.

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